

**REMARKS**

Reconsideration is requested.

Claims 1-12 and 30-62 are pending. Claims 1-12 have been withdrawn from consideration however rejoinder of the same is requested once allowable product claims are found. Claims 1-12 have been amended above to be dependent on the pending product claims to advance prosecution and rejoinder of the method claims. The Examiner is requested to allow the applicants the opportunity to make any further amendments which may be required, at an appropriate time, to facilitate rejoinder of the method claims.

Claims 44, 52 and 53 have been allowed. Claims 44 and 53 (and 43) have been rewritten for clarity. Claims 44, 52 and 53 are believed to be allowable, as well as the remaining claims, for the reasons noted below.

Claim 30 has been amended to emphasize the substantial non-protein nature of the presently claimed antigenic source and to further distinguish the claimed invention over the cited art. Support for the amendment to claim 30 may be found in the second paragraph on page 16 of the specification. Claim 42 has been amended for clarity and is based on, for example, the third paragraph on page 19 of the specification. The unamended claims 44, 45 and 53 have been added as new claims 54, 55 and 62. New claim 56, which is dependent on claim 47, also emphasizes the substantial non-protein nature of the presently claimed antigenic source. Claims 57 and 58 are similar to claim 52 while reciting the fungus of claim 43 and allowed claim 44, respectively. Finally claims 59-61 are directed to methods of claim 1 wherein the fungal cell culture

supernatant is specifically identified as the fungi of claims 43, 44 and 52. No new matter has been added.

The Examiner is requested to acknowledge receipt of the certified copy of the priority document, which was submitted October 17, 2001, in the Examiner's next Action.

The Section 102 rejection of claims 30-36, 40-41 and 45-46 over Pasarell (Journal of Clinical Microbiology, July 1990, pages 1655-1657, Vol. 28, No. 7), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

Initially, the applicants note that Pasarell used an Amicon PM10 filter (page 1665, right column, at the end of the first full paragraph of the cited reference) which will discard anything in the filtrate that is less than 10,000 m.w. while retaining large proteins. The presently claimed invention however provides a fungal cell culture supernatant containing fungal or yeast components shedded to the supernatant during culturing. That is, the presently claimed invention defines a supernatant which has retained all or substantially all of the components in the supernatant, such as, for example, aflatoxins which have a molecular weight, for example, of less than 400 m.w. Accordingly, the cited reference fails to teach each and every aspect of the presently claimed invention and the Section 102 rejection of claims 30-36, 40-41 and 45-46 should be withdrawn.

Moreover, the Examiner appears to suggest that the reference teaches cross-reaction between fungal antigens. However, the applicant believes that the cited reference teaches at page 1656 on the left column, second paragraph that antigens

from several bacteria do not cause react. Page 1656, right column, in the first full paragraph, of the cited reference notes that where cross-reaction did occur it was likely due to the existence of the single ascomycetous genus *Cochliobolus* containing anamorphs classified in both the genera *Bipolaris* and *Curvularia*. The cited reference therefore is believed to teach away from the presently claimed and disclosed invention.

Withdrawal of the Section 102 rejection of claims 30-36, 40-41 and 45-46 over Pasarell is requested.

The new Section 102 rejection of claim 43 over Pasarell should be withdrawn for similar reasons.

The Section 102 rejection of claim 30-35, 41 and 46 over Calera (Infection and Immunity, June 1994, pages 2322-2333, Vol. 62, No. 6), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

As the Examiner has pointed out, the antigens used in Celera reference identified only *Aspergillus* species. There is no evidence of any cross-reaction to different genus as is presently claimed.

The Examiner has requested a side-by-side comparison to demonstrate a difference between the claimed invention and the teaching of Calera. The applicant urges the Examiner to appreciate that several aspects of the disclosure of the cited art highlight the differences between the art and the claimed invention such that further comparisons should not be required. Specifically, Calera was able to freeze and freeze-dry their samples (page 2324) with apparently limited or no detrimental effect. The applicant has not been able to freezer or freeze dry the composition of the invention.

This is not to say that a cryoprotectant could not be added to freeze the presently claimed product however Calera apparently required no such protectant. Calera dialyzed their freeze dried preparation (page 2324, first column, middle) which will remove components less than 8,000 m.w. while the applicant has disclosed the advantage of retaining lower molecular weight components. Calera focuses in proteins from 14,000 - 200,000 m.w. with most being 25,000 to 97,000 m.w. (page 2327, second column) whereas the presently claimed invention is minimally effected by proteinase, which would be expected to destroy the composition of Calera. Finally, Calera is understood to teach that supernatant antigens were useless. See, page 2327, second column. Most of the work of Calera is believed to have been based on whole cell or filtered and washed "wet cake" (see, page 2324, first column, third paragraph).

Moreover, the Examiner is urged to appreciate, for example, that Table VII of the present application demonstrates that serum from mice vaccinated with *Ulocladium* fungal cells reacts with a plate coated with *Bipolaris* supernatant antigens with a 7-fold greater sensitivity than if *Ulocladium* antigens were used. This evidence is a dramatic example of the surprising utility and difference of the presently claimed invention.

Withdrawal of the Section 102 rejection of claims 30-35, 41 and 46 over Calera is requested.

The Section 102 rejection of claims 30-35, 37-39, 41 and 45-46 over Takesako (U.S. Patent No. 6,333,164), is traversed. Reconsideration and withdrawal of the rejection are requested as the applicants submit that the fungal antigens of Takesako appear to be proteins. Such proteins would be damaged by proteinases to a great extent such that the presently claimed invention does not define the product of

Takesako. Reconsideration and withdrawal of the Section 102 rejection of claims 30-35, 37-39, 41 and 45-46 over Takesako is requested.

Claims 30-36, 41-42 and 45-51 over van der Heide is traversed.

Reconsideration and withdrawal of the restriction are requested.

The applicant notes that the antigens of van der Heide were prepared according to Reference 6 of the cited reference. Reference 6 in the cited reference is van der Heide et al. (Allergy 40, 586-591, 1985). The preparation method of the reference should be available to the Examiner however the applicant would be happy to submit the same upon further request by the Examiner. The applicant notes that the method of the Reference 6 teaches the use of an H4P5 hollow fiber Amicon filtration (page 587, first column, at the bottom) which would be understood by one of ordinary skill in the art to reduce low molecular weight components. As explained above however the applicant has claimed the composition wherein the low molecular weight components are important and present. Moreover, the dialysate of van der Heide is frozen or freeze dried whereas such a procedure would inactivate the presently claimed product, without the use of cryo protectants. Finally, the Reference 6 of van der Heide suggest that the antigens of the cited reference are proteins as the reference states at page 589, second column, at the top that during Phase I an excretion of proteins was observed. As noted previously, proteins are, at most, a minor component of the presently claimed invention as only a minor reduction in activity is found with proteinase digestion. Accordingly, the claims are submitted to be patentable over van der Heide.

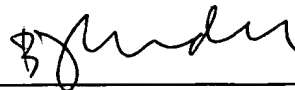
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The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is urged to contact the undersigned in the event anything further is required in this regard.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: \_\_\_\_\_



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